

**REMARKS**

Claims 18-31, 55-117, 120, 121, and 126-129 have been cancelled without prejudice or disclaimer. Claims 2 and 45 have been amended. Claims 152-153 are new. Support for the claim amendments can be found through the specification. No new matter has been added.

Upon entry of this amendment, claims 1-17, 32-54, 118, 119, 122-125, and 147-153 are pending in this application. Claims 5, 6, 8, 10, 14-16, 32-43, 48, 49, 51, 53, 118, 122, and 124 stand withdrawn from consideration.

Applicants respectfully reserve the right to pursue any non-elected, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

Applicants request reconsideration of the application in view of the amendments and arguments herein. Rejections of cancelled claims are deemed moot and are not further discussed herein.

**Interview Summary**

Applicants thank the Examiner for the courtesy of a telephonic interview with one of their undersigned representatives on October 15, 2007. During the Interview, the rejection under 35 USC §103(a) was discussed. Applicants' representative proposed submitting a Declaration Under 37 CFR 1.132. No final agreement was reached.

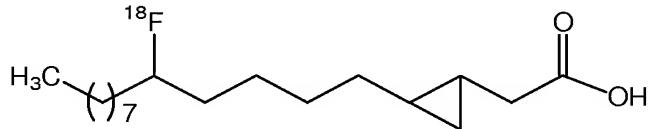
**Rejections under 35 U.S.C. § 103**

Claims 1-4, 7, 9, 11-13, 17, 44-47, 50, 52, 119, 123, 125 and 147-151 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over International Patent Publication No. WO 97/19705 to Elmaleh ("Elmaleh"), in view of United States Patent No. 4,323,547 to Knust, *et al.* ("Knust") and No. 4,524,059 to Elmaleh ("US-Elmaleh"). This rejection is traversed.

The teachings of the Elmaleh, Knust, and US-Elmaleh references have been described previously (in the papers filed March 12, 2007, and July 20, 2007, which are incorporated herein by reference). For at least the reasons described in the papers filed March 12, 2007, and July 20, 2007, none of the cited references, alone or in combination, renders obvious the pending claims.

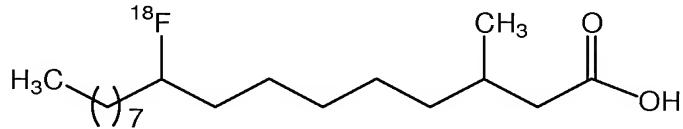
Moreover, Applicants contend that, even if the Examiner had made out a *prima facie* case of obviousness (which Applicants dispute), unexpected results rebut any such *prima facie* case.

For example, as discussed in the enclosed Declaration Under 37 CFR 1.132 of David Elmaleh, Ph.D. (hereinafter “the Declaration”), the compounds of the Application have unexpectedly superior properties compared to the compounds of the cited references. For example, the present Application discloses and claims the compound [<sup>18</sup>F]-9-fluoro-3,4-cyclopropylheptadecanoic acid (see, e.g., claim 147), represented by the structure:



This compound, hereinafter referred to as [<sup>18</sup>F]FCPHA, has a cyclopropyl ring located at the 3,4-position (that is, the cyclopropyl moiety includes carbon atoms 3 and 4 of the fatty acid chain).

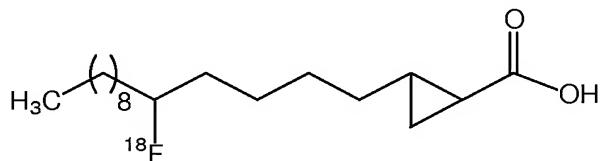
The Elmaleh references cited by the Examiner contemplate certain labeled  $\beta$ -methyl-substituted fatty acids. Applicants submit that an exemplary compound is [<sup>18</sup>F]-9-fluoro-3-methylheptadecanoic acid (not specifically disclosed in the Elmaleh references), hereinafter referred to as [<sup>18</sup>F]FBMHA, represented by the structure:



The only difference between [<sup>18</sup>F]FCPHA and [<sup>18</sup>F]FBMHA is the presence of a 3,4-cyclopropyl group in [<sup>18</sup>F]FCPHA rather than a 3-methyl group in [<sup>18</sup>F]FBMHA.

As described in the Declaration, experiments were performed to compare the properties of [<sup>18</sup>F]FCPHA and [<sup>18</sup>F]FBMHA. It was found that the heart-to-tissue ratios for the two compounds are significantly different. In particular, the heart-to-blood ratio for the compound of the present claims (<sup>[18]F</sup>FCPHA) is much higher than the corresponding ratio for <sup>[18]F</sup>FBMHA (about 10-fold at 5 minutes, and more than 6-fold at 60 minutes). This is important because the diagnostic capability of an imaging agent (such as a cardiac imaging agent) can be improved by improving the target-to-non-target tissue ratio.

In a similar manner, experiments were performed to test the corresponding 2,3-cyclopropyl fatty acid [<sup>18</sup>F]-8-fluoro-2,3-cyclopropylheptadecanoic acid (2,3-CP-8-[<sup>18</sup>F]-FA) (a compound related to the generic disclosure of the Elmaleh PCT application as described above), represented by the structure:



The only difference between [<sup>18</sup>F]FCPHA and the 2,3-cyclopropyl analog is the presence of a 3,4-cyclopropyl group in [<sup>18</sup>F]FCPHA rather than a 2,3-cyclopropyl group in 2,3-CP-8-[<sup>18</sup>F]-FA, and the radiolabel is on the 8-carbon in 2,3-CP-8-[<sup>18</sup>F]-FA rather than the 9-carbon in [<sup>18</sup>F]FCPHA. It will be appreciated that the F-18 radiolabel (at C-8) of 2,3-CP-8-[<sup>18</sup>F]-FA is at the same distance from the cyclopropyl group (5 carbon atoms) as the F-18 radiolabel on [<sup>18</sup>F]-9-fluoro-3,4-cyclopropylheptadecanoic acid (<sup>[18]F</sup>FCPHA) and the methyl analog described above (<sup>[18]F</sup>FBMHA).

As discussed in the Declaration, the uptake of 2,3-CP-8-[<sup>18</sup>F]-FA into heart is poor compared to uptake into liver. As described in the Declaration, the heart-to-blood ratio for the compound of the present claims (<sup>[18]F</sup>FCPHA) is much higher than the corresponding ratio for 2,3-CP-8-[<sup>18</sup>F]-FA (about 12-fold at 5 minutes, and more than 5-fold at 60 minutes), showing that the compound according to the present claims has increased myocardial uptake and kinetics. As previously discussed, a compound having a higher heart-to-blood ratio and/or higher heart-to-liver ratio and/or higher heart-to-lung ratio should have increased tissue selectivity and improved heart image resolution and diagnostic accuracy.

As discussed in the Declaration, it is unexpected and surprising that a compound of the present claims would have higher heart-to-tissue ratios than the compounds described above corresponding to the references cited by the Examiner. For this additional reason, Applicants contend that the cited references, whether considered alone or in any combination, cannot render obvious the pending claims.

Reconsideration and withdrawal of the rejection is proper and the same is requested.

### CONCLUSION

For at least the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of all rejections and allowance of the application with all pending claims. If a telephone conference with Applicants' representative would be helpful in expediting prosecution of the application, the Examiner is invited to call either of the undersigned representatives at the telephone number indicated below.

Although it is believed that no extension of time is required, Applicants conditionally petition for any extension of time required for consideration of this response. Applicants do not believe that any further fees are required for consideration and entry of this Amendment and Response. Nevertheless, the Director is authorized to charge any required fee or credit any overpayment to Deposit Account No. 04-1105 under order number 62041(51588).

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Respectfully submitted,

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